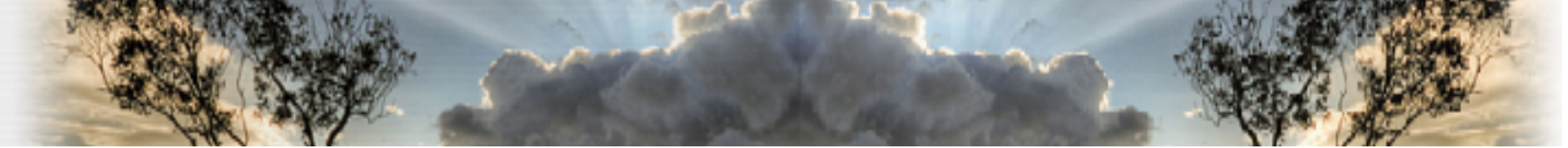

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A recent EBF survey on regional barriers

Cecilia Arfvidsson, on behalf of the EBF

Introduction

We hear **increased worries** on how (we think) **barriers** are created across the bioanalytical globe affecting how we work e.g. due to:

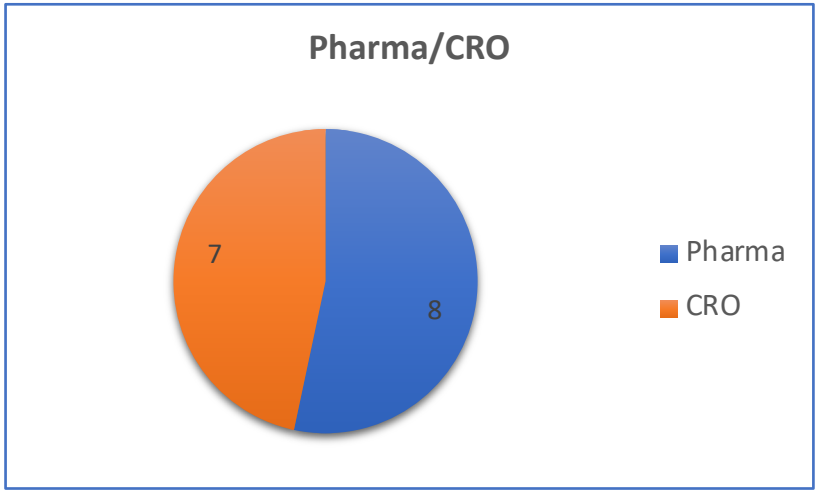
- new/emerging guidelines
- different interpretation of guidelines in regions, either by industry or by regulators
- intensified global R&D

We wanted to **name them** to potentially facilitate in the **resolution** of some of them…

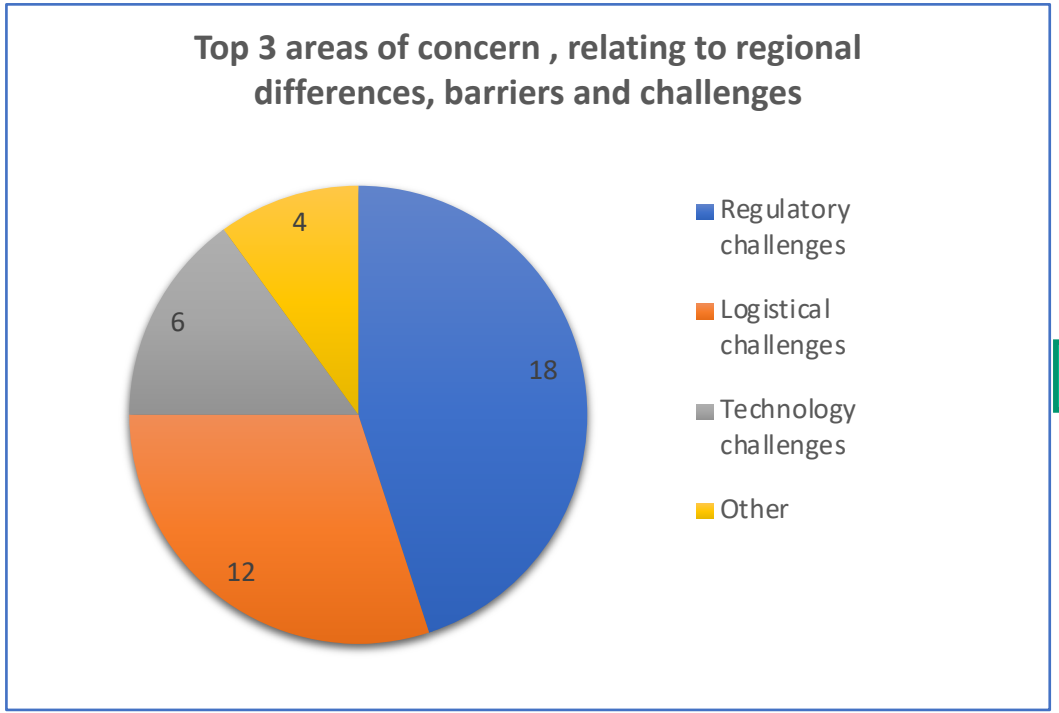
Finger on the Pulse Survey

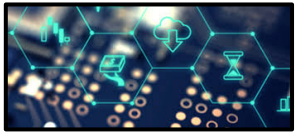
- A finger on the pulse (**FotP**) survey was therefore sent out to all EBF core members
- "*Please list your **top 3 areas** of concern relating to regional differences, barriers and challenges*"

- We received feedback from 15 core members, representing both Pharma and CRO



Survey Responses





Same 3 areas of concern highlighted

Regulatory challenges

Different interpretation of **GCP requirements** in different countries (e.g. EMA, MHRA, FDA).

What does Brexit bring? (More) "**MHRA vs EU" guidelines**, different expectations with respect to eg GCP, GLP compliance of nonclinical data sets etc. …

Differences in HA expectations regarding **co-med stability testing**

Regulatory challenges/differences such as:
- **ANVISA requirements** for certification of labs for BE studies
- **FDA requirements** regarding MD data
- Differences in acceptable A&P criteria for biologics by mass spec between FDA and ROW
- Application of **draft ICH M10**
- biomarker regs – patient care (CLIA/ISO115189) vs BMV

Region-specific guidelines are still being **drafted** (eg latest China immunogenicity draft; no public english version available, extremely short review time almost preventing the globe from commenting), and all this in light of other attempts (ICH M10) to **harmonise guidelines** and go away from region-specific guidelines…

Regulatory challenges

Filing documentation - different regions seem to have **different templates** they would like to have submission relevant information (eg on validated method) in

The **different level of knowledge** of the **reviewers** of our submissions. **Box checkers** asking questions just for the sake of asking them vs folks who understand the bioanalytical science

Supplementary submission materials that are required for **specific countries**. Best known example of this is the CS-BE required by Health Canada for not only bioequivalence studies but also food effect studies.

Differences in **regulatory guidance expectation and inspection approach** certainly features high for me. Regulatory **differences driving differences in approach** around the world and perhaps even the **perception** that in geographies where regular inspection is part of being in a regulated program there is **better quality**. I expect there are still many small CRO and small pharma labs that **claim compliance** but have **never been inspected** as they do not support BE studies in the US.

Logistical challenges

Shipping **samples out of China** (likely many have this)

Logistical Challenges:
assay/reagents/sample transfer with China. Difficulties in getting things **into China**, but even more difficult to get **things out**.

Export/import Non-human samples from France to US or from US to France (CITES need)

Sample logistics in general but particularly from **overseas**, most likely due to the **Corona pandemic** (reduced number of flights, higher customs hurdles).

Barriers (CITES, USDA) limiting free import/export of **NHP samples**.

Increased hurdles for PK **sample shipment out of China** to BA CROs located outside of China making it impossible to analyze all samples from 1 study in 1 lab thus requiring **in-study x-validations**; **increased hurdles/paperwork** for importing samples into China for crossvalidation purpose

Technical challenges

Method transfer of **complex workflows** in a world where assays become increasingly **platform specific**

There is a **chicken and egg situation** with some new technology. Pharma will purchase and use but there is little availability at CRO to transfer unless a specific vendor requests this. So some tech availability externally has a long lead time.

Differences in **skills** between regions

Access to **approved technology in a region**….I'm thinking of CE marking and such can **limit the utility around the globe**, certainly for very new kit that has proven an issue in the past.

Method transfer … capturing all the **nuances** which may be important but seemingly innocuous, I think can often be a challenge. These **small details can really come to the fore** in different parts of the world

Complicated assays need to be set up in **China based BA labs** which requires a **lot of effort/discussions** eg siRNA assays with complicated patent discussions; plasma protein binding determinations where the **CROs have no experience** with equilibrium dialysis, biomarker determinations when assay reagents are not available in China…

Other challenges

Personnal data protection between US and Europe.

Impact of **Brexit**

Language is key……are things lost in translation?

Timezones can give you positive advantages and negative ones…..having **geographical alignment** of labs to where our studies are conducted can give us agility…..**managing labs** and the **conversations** between labs in different timezones can be **less efficient** since we are waiting longer for replies sometimes.

Summary

Current regional barriers and challenges are focused to **3 top areas:**

- **Regulatory differences** due to exciting/new regional guidance and/or regional interpretations of the guidance
- **Regulatory differences** in the different filing templates required and/or the differences in expectations on the data to be included in a submission file
- **Logistical challenges**, especially all logistics (samples, reference material, critical reagents…) in and out of China
- **Technical challenges** due to regional differences in expertise skills and availability of specific technology/platforms

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